

Amendments to the Specification:

Please replace the last paragraph on page 4 spanning the top of page 5 with the following amended paragraph:

In the present invention it was found that macrophages involved in an inflammatory process, particularly in a chronic inflammatory airway disease, more particularly in chronic bronchitis or COPD, show a pattern of differentially expressed nucleic acid sequence and protein expression which differs from the pattern of gene expression of macrophages from healthy donors or donors in an irritated state, which latter do contain macrophages in an activated state. Therefore, macrophages show different activation levels under different inflammatory conditions. For example, it is shown in the present invention that macrophages involved in an inflammatory process in COPD smokers show different gene expression pattern than macrophages from healthy smokers, indicating that in COPD smokers macrophages are in a different, hereinafter named "hyperactivated" or "hyperactive" state. The present invention provides for the inhibition of the hyperactivation or the reduction of the hyperactive state of a macrophage by the identification of substances which modulate a protein selected from the group consisting of MIF (Calandra, T. *et al.* (1994) J. Exp. Med. 179, 1985-1995-1902; Bernhagen, J. *et al.* (1998) J. Mol. Med. 76, 151-161; Calandra, T. *et al.* (2000) Nat. Med. 6, 164-170), DAD1 (Nakashima, T. *et al.* (1993) Mol. Cell. Biol. 13, 6367-6374; Kelleher, D., and Gilmore, R. (1997) Proc. Natl. Acad. Sci. U.S.A. 94, 4994-4999), ARL4 (Jacobs, S. *et al.* (1999) FEBS Lett. 456, 384-388), GNS (Kresse, H. *et al.* (1980) Proc. Natl. Acad. Sci. U.S.A. 77, 6822-6826), Transglutaminase 2, (Folk, J.E. (1980) Annu. Rev. Biochem. 49, 517-531; Lu, S. *et al.* (1995) J. Biol. Chem. 270, 9748-9756). Stearyl-CoA-Desaturase (Enoch, H.G. *et al.* (1976) J. Biol. Chem. 251, 5095-5103) and UDP-Glucose Ceramide Glycosyltransferase (Basu, S. *et al.* (1968) J. Biol. Chem. 243, 5802-5807; Ichikawa, S. *et al.* (1996) Proc. Natl. Acad. Sci. U.S.A. 93, 4638-4643), all depicted in the Sequence Listing hereinafter, involved in the hyperactivation or maintaining the hyperactive state of a macrophage.